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Experience in the Treatment of Synchronous and Metachronous Carcinoma of the Oesophagus and the Head and Neck

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Background and Objectives: Treatment of multiple primary squamous cell carcinomas of the head and neck and oesophagus is controversial. The poor prognosis of these 2 types of carcinoma taken individually and their anatomic proximity complicate the therapeutic strategy and limit the treatment choices for each location.

Methods: From 1986 to 1998, 43 patients received curative treatment for multiple synchronous (n = 30) or metachronous (n = 13) primary neoplasms of the oesophagus and head and neck. For synchronous cancers, the therapeutic strategy consisted of first curing the head and neck cancer and then planning oesophagectomy according to the type of head and neck cancer therapy.

Results: Ten total oesopharyngolaryngectomies and 33 subtotal oesophagectomies were performed. The postoperative mortality rate was 9.3% (4/43). The rate of anastomotic leakage was 30% (13/43), and all such leaks were cervical. Pulmonary infection occurred in 19% of cases (8/43). A past history of cervical radiation therapy or cervicotomy did not appear to be a significant risk factor for anastomotic leakage or pulmonary complications. Oesophagectomy did not affect the functional results in the 31 patients whose larynx could be preserved.

Conclusions: Oesophagectomy after head and neck cancer treatment is possible with a low mortality rate and acceptable morbidity.

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KEY WORDS: **oesophageal carcinoma; head and neck cancer; multiple carcinomas; oesophageal surgery**

INTRODUCTION

Drinking and smoking are epidemiological risk factors for squamous cell carcinomas of the head and neck and the oesophagus [1–3] and account for the high incidence of the combination [4,5]. Moreover, in patients with head and neck cancer, routine endoscopy of the oesophagus at diagnosis [6,7], long-term post-therapeutic follow-up, and improved survival after treatment [8] result in more frequent detection of second primary carcinoma of the oesophagus [9,10]. There have been very few studies focusing on curative therapeutic strategies for such patients, and treatment options are controversial [11,12]. The poor prognosis of these 2 types of carcinoma taken individually and their anatomic proximity complicate the therapeutic strategy and limit the treatment options for each location [13]. Confronted with an increasing number of such cases, we devised a basic therapeutic plan that consists of first curing the head and neck cancer. This study was conducted to determine the immediate outcome of oesophagectomy after treatment for meta-

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TABLE I. Clinical and Pathological Background of 43 Patients with Oesophageal and Head and Neck Cancers

	Synchronous group (n = 30)	Metachronous group (n = 13)	Total (n = 43)
Sex ratio (M/F)	26/4	13/0	39/4
Age (years)	54.5 ± 7	61 ± 6	56.5 ± 7
Oesophageal tumour location			
Upper oesophagus	8	4	12
Middle oesophagus	19	9	28
Lower oesophagus	3	—	3
Oesophageal cancer TNM staging			
No residual tumor	5	—	5
Stage I	9	1	10
Stage IIa	6	8	14
Stage IIb	2	2	4
Stage III	6	2	8
Stage IV	2[a]	—	2

[a]Coeliac node involvement.

TABLE II. Distribution of Synchronous and Metachronous Head and Neck Cancers

	Synchronous group (n = 30)	Metachronous group (n = 13)	Total (n = 43)
Oral cavity	5	7	12
Tongue	—	3	3
Tonsillar fossa	1	—	1
Floor of mouth	6	2	8
Oropharynx	12	4	16
Tonsil	7	1	8
Base of tongue	2	1	3
Soft palate	2	2	4
Uvula	1	—	1
Larynx	4	9	13
Vestibula	4	5	9
Glottis	1	4	5
Hypopharynx	11	3	14
Total	32	23	55

chronous or synchronous cancer of the head and neck.

MATERIALS AND METHODS

Patients

Between January 1986 and April 1998, a total of 43 consecutive patients underwent potentially curative treatment for multiple primary carcinomas of the head and neck and oesophagus. Tumours were defined as synchronous or metachronous if the diagnostic interval between the 2 cancers was, respectively, less or more than 6 months. Thirty patients had a head and neck cancer synchronous with an oesophageal carcinoma; 3 of these patients had previously been treated for head and neck cancer. Thirteen patients had metachronous head and neck cancer; the head and neck cancer always developed before the oesophageal cancer, and the mean diagnostic interval between the 2 malignancies was 5 ± 3.5 years (range 1–14). All patients with metachronous lesions were in remission from the head and neck cancer at the time of oesophagectomy. Clinical characteristics are shown in Table I. Histological features of the oesophageal cancers were defined according to the TNM classification [14]. At diagnosis, 7 patients had more than 2 lesion sites: 3 patients had 2 carcinomas of the oesophagus and 1 patient had 3; 4 patients had 2 synchronous tumours of the head and neck. Details of the head and neck cancer locations are given in Table II.

Therapeutic Strategy for Synchronous Head and Neck Cancers

For synchronous cancers, the therapeutic strategy consisted of first curing the head and neck cancer and then planning oesophagectomy according to the type of head and neck cancer therapy. Patients were divided into 4 groups, depending on the treatment of the head and neck cancer, as follows: group 1, head and neck cancer exclusively treated with radiation therapy and/or chemotherapy; group 2, head and neck tumour resected by the peroral approach; group 3, major head and neck surgery with cervicotomy; group 4, total oesopharyngolaryngectomy. In the interval between the treatment of the 2 cancers, patients with severe weight loss or dysphagia received enteral nutrition.

Oesophageal Resection

Oesophagectomy was performed either via a fifth intercostal space right thoracotomy with posterior mediastinectomy or via a transhiatal approach after ventral phrenotomy. Oesophageal reconstruction was preferably achieved with a tube formed from the great curvature of the stomach. The colon was used when the stomach was not available. A pyloroplasty and a feeding jejunostomy were constructed in every case. Oesophagogastric terminolateral anastomosis was routinely hand-sewn at the cervical level or constructed using a circular stapler in the thorax.

Chemotherapy and Radiation Therapy

All patients with synchronous lesions received neoadjuvant chemotherapy for their head and neck cancer (2 or 3 courses of 5-fluorouracil and cisplatin). Cervical radiation therapy consisted of external 45-Gray cobalt therapy or curietherapy. None of the patients received neoadjuvant chemoradiotherapy for their oesophageal cancer.

Evaluation

The analysis focused on the therapeutic strategy, postoperative complications after oesophagectomy, the time required for resumption of oral feeding, the length of

TABLE III. Management of Synchronous and Metachronous Head and Neck Cancers

	Synchronous group (n = 30)	Metachronous group (n = 13)	Total (n = 43)
Exclusive chemoradiotherapy	3	2	5
Peroral approach	10	6	16
Oropharyngectomy and mandibulectomy	3	2	5
Partial laryngectomy	1	5	6
Total laryngectomy	—	1	1
Partial pharyngolaryngectomy	4	1	5
Total pharyngolaryngectomy	2	2	4
Total oesopharyngolaryngectomy	9	—	9

hospital stay, and preserved phonation and swallowing functions in patients with conservative or reconstructive surgery.

Statistical Analysis

Data are given as means ± 1 standard deviation. Differences between groups of patients were compared using the Mann-Whitney *U*-test or the χ^2 test, with Yates correction if necessary. A P value of <0.05 was regarded as statistically significant.

RESULTS

All patients underwent potentially curative treatment of their head and neck and oesophageal carcinomas.

Treatment of Head and Neck Cancers

Five head and neck cancers were treated by chemotherapy and/or radiotherapy exclusively, 16 by endobuccal surgery, 21 by major head and neck surgery with cervicotomy, and 9 by total oesopharyngolaryngectomy (Table III). When the head and neck cancer was treated by chemoradiotherapy or endobuccal surgery, oesophagectomy was delayed by approximately 4 weeks and adjuvant cervical lymph node dissection, when necessary, was performed at the cervical time of oesophagectomy. For patients with major head and neck surgery, oesophageal resection was delayed by 2 months. Prior to oesophagectomy, 9 metachronous patients and 12 synchronous patients underwent cervicotomy for head and neck cancer resection and 6 metachronous patients and 5 synchronous patients received cervical radiation therapy exclusively or as an adjuvant for their head and neck cancer treatment. Three patients had severe adverse effects of radiotherapy involving the cervical tissue.

Treatment of Oesophageal Cancer

Thirty-three patients underwent subtotal oesophagectomy, and 10 patients underwent total oesopharyngolaryngectomy (Table IV). The indications for total oesopharyngolaryngectomy were piriform sinus cancer (n = 9) and cervical cancer of the oesophagus (n = 1). Among the 33 patients who underwent subtotal oesophagectomy, the oesophageal substitute was anastomosed to the cervical oesophagus in 28 patients and to the upper thoracic oesophagus in 5. The reasons for performing cervical anastomosis were that the tumour was located in the upper part of the oesophagus or dissection of the cervical lymph nodes. Three of the 5 patients who underwent intrathoracic oesogastric anastomosis should, however, have undergone cervical anastomosis, given the location of the oesophageal cancer. The reason for changing the level of the anastomosis was adverse effects of radiotherapy on cervical tissue in 2 cases and the presence of a jejunal transplant in 1.

Mortality and Morbidity of Oesophagectomy

Mortality and morbidity are shown in Table V. Four of 43 patients (9.3%) died in the postoperative period, 2 of liver dysfunction (patients with cirrhosis), 1 of pulmonary infection, and 1 of massive coronary thrombosis. Anastomotic leakage occurred in 13/43 patients, always at the cervical level. In 12 patients, the leakage dried up within 2 weeks. In 1 patient, the cervical anastomotic leakage was complicated by a mediastinal collection that was successfully treated by percutaneous drainage. The time required to resume oral feeding was significantly longer ($P = 0.0167$) in the synchronous group, but the length of hospital stay was similar in the 2 groups. Pulmonary infection occurred in 8/43 patients (18%). A past history of cervical radiation therapy and previous cervicotomy did not appear to be significant risk factors for anastomotic leakage or pulmonary complications (Table VI).

Eight (28%) of the 29 patients without permanent tracheostomy had temporary tracheotomy following oesophagectomy because of the need for prolonged artificial ventilation. After treatment of the head and neck and oesophageal cancers, larynx preservation was achieved in 29 patients (72%). All recovered their preexisting phonation and swallowing functions after oesophagectomy.

DISCUSSION

Treatment of oesophageal cancer is often influenced by the combined presence of head and neck cancer, a combination carrying a grim prognosis. Moreover, given the anatomic proximity of the organs involved, the treat-

TABLE IV. Operative Techniques for Oesophagectomy

	Synchronous group (n = 30)	Metachronous group (n = 13)	Total (n = 43)
Subtotal oesophagectomy	20	13	33
Approach			
Right thoracotomy	8	10	18
Transhiatal	11	4	15
Reconstruction			
Gastric tube	19	12	31
Colon	1	1	2
Anastomosis			
Cervical	17	11	28
Thoracic	3	2	5
Total oesopharyngolaryngectomy	10	—	10

TABLE V. Mortality and Morbidity after Oesophagectomy

	Synchronous group (n = 30)	Metachronous group (n = 13)	Total (%) (n = 43)
Postoperative mortality	2	2	4 (9)
Anastomotic leakage	10	2	12 (28)
Pneumonia	7	1	8 (19)
Pulmonary oedema	1	—	1 (2.5)
Recurrent nerve paralysis	3	—	3 (7)
Subclavian venous thrombosis	—	3	3 (7)
Acalculous cholecystitis	—	1	1 (2)
Pericardial effusion	—	1	1 (2)
Time to oral feeding (days)	20 ± 15	10 ± 4	18 ± 14
Hospital stay (days)	28 ± 14	29 ± 14	28 ± 14

TABLE VI. Analyses of Factors That Could Potentially Increase Occurrence of Anastomotic Leak and Pneumonia after Oesophagectomy in the Synchronous and Metachronous Groups

	Synchronous group (n = 30)	Metachronous group (n = 13)	Total (%) (n = 43)
Anastomotic leaks	10/30	2/13	12/43 (28)
Radiotherapy			
Yes	1/5	1/6	2/11 (18)
No	9/25	1/7	10/32 (31)
Prior cervicotomy			
Yes	5/13	1/10	6/23 (26)
No	5/17	1/3	6/20 (30)
Reconstruction			
Gastric tube	8/21	2/11	10/32 (31)
Colon	2/9	0/2	2/11 (18)
Oesophagectomy			
Subtotal	9/20	2/13	11/33 (33)
Total OPL[a]	1/10	—	1/10 (10)
Pneumonia	7/30	1/13	8/43 (19)
Radiotherapy			
Yes	2/5	0/6	2/11 (18)
No	5/25	1/7	6/32 (19)
Prior cervicotomy			
Yes	2/13	1/10	3/23 (13)
No	5/17	0/3	5/20 (25)
Anastomotic leaks			
Yes	3/10	0/2	3/12 (25)
No	4/20	1/11	5/31 (16)
Oesophagectomy			
Subtotal	4/20	1/13	5/33 (15)
Total OPL	3/10	—	3/10 (30)

[a]OPL, oesopharyngolaryngectomy. Differences were not significant.

ment of head and neck cancer by surgery or radiation therapy may limit the therapeutic possibilities for oesophageal cancer. Thus, the surgical indications are often more limited than for solitary oesophageal carcinomas [15,16].

In metachronous cancers, the mean interval between the diagnosis of head and neck cancer and oesophageal cancer ranges from 4 to 5 years [15,17,18]. Consequently, at the diagnosis of oesophageal cancer, the head and neck cancer is generally considered cured. In such cases, factors that complicate surgery of the oesophagus are a previous history of cervical surgery and/or cervical radiation therapy when cervical anastomosis is required. In patients with previous anterior pharyngolaryngectomy in whom the oesophageal substitute has to be anatomosed to the remaining upper thoracic oesophagus, care must be taken to respect the vessels connecting the trachea and the upper oesophagus and to not damage the vasculature of the remaining oesophagus [12].

In synchronous cancers, the problem can be 2-sided: either total oesopharyngolaryngectomy is necessary for optimal treatment of both locations or each cancer can be treated separately, which raises a problem of timing. Treatment of the head and neck cancer first, by means of surgery or cervical radiation therapy, might theoretically worsen the morbidity of subsequent oesophagectomy. The cervical approach may be more difficult, and the risk of anastomotic leakage and recurrent nerve paralysis is potentially increased. Such factors may induce a higher incidence of postoperative pulmonary complications, which account for the bulk of mortality and morbidity following oesophagectomy [19,20]. In our study, the only complication that was more frequent in the synchronous group was cervical anastomotic leakage, a finding

possibly explained by the recent cervicotomy. When permitted by the location of the oesophageal tumour, intrathoracic oesophagogastric anastomosis avoids the disadvantages of repeated cervicotomy and, therefore, shortens the interval between head and neck and oesophageal surgery.

Initial head and neck treatment can also delay oesophagectomy and thus allow the oesophageal tumour to progress. Neoadjuvant therapy might be considered in this interval between the 2 treatments. However, preoperative chemoradiotherapy for oesophageal cancer does not improve overall survival and may increase the mortality rate after oesophagectomy [21]. In our series, none of the oesophageal tumours became nonresectable in the interval after head and neck cancer treatment. On the contrary, the interval allowed us to conduct oesophagectomy in selected patients whose general condition had been improved by weight gain and tobacco and alcohol withdrawal.

Oesophageal resection as the first-step therapy has similar disadvantages as it carries its own postoperative complications that can also compromise or delay the treatment of the head and neck cancer. We opted for initial treatment of the head and neck cancer and performed oesophagectomy only in patients whose head and neck cancer could be locally controlled. Oesophagectomy was delayed, to avoid adding its complications to those of the head and neck cancer surgery. The length of this interval depended on the degree of head and neck cancer treatment. It was generally short after chemoradiotherapy or endobuccal surgery. In contrast, following major head and neck surgery (e.g., transmandibular oropharyngectomy or partial pharyngolaryngectomy), a 2- to 3-month interval before oesophagectomy was necessary for complete cervicotomy healing and for the patient to recover sufficient pulmonary and swallowing capacities. This multistage surgery, despite the higher rate of anastomotic leakage, tended to permit more conservative surgery for these multiple carcinomas of the head and neck and the oesophagus. Oesophagectomy after head and neck cancer treatment had an acceptable morbidity and mortality rate in this series.

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